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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/729,027	12/05/2003	Xin-Xing Gu	NIH142.1CDV1	8829
45311	7590	08/10/2005		
KNOBBE, MARTENS, OLSON & BEAR, LLP 2040 MAIN STREET FOURTEENTH FLOOR IRVINE, CA 92614				
			EXAMINER	
			FORD, VANESSA L	
			ART UNIT	PAPER NUMBER
			1645	

DATE MAILED: 08/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No.	Applicant(s)
	10/729,027	GU ET AL.
	Examiner	Art Unit
	Vanessa L. Ford	1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) Responsive to communication(s) filed on 18 May 2005.
- 2a) This action is FINAL.                            2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) Claim(s) 23-28 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 23-28 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on 05 December 2003 is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All    b) Some \* c) None of:
  1. Certified copies of the priority documents have been received.
  2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                    | Paper No(s)/Mail Date. _____.   |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____. | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
|   | 6) <input type="checkbox"/> Other: _____.                                   |

## **DETAILED ACTION**

1. This action is responsive Applicant's response filed May 18, 2005. It should be noted that a new Examiner is examining this application. A new grounds of rejection is set forth below.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office Action.

### ***Rejection Withdrawn***

3. In view of Applicant's response the rejection of claims 23-28 under U.S.C. 103(a), pages 2-3, paragraph 6 has been withdrawn.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 23-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for method of making an immunogenic composition comprising a detoxified lipooligosaccharide covalently linked to an immunogenic carrier does not reasonably provide enablement for making a conjugate vaccine against *Moraxella catarrhalis* comprising a detoxified lipooligosaccharide covalently linked to an

immunogenic carrier. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant specification teaches that the conjugate vaccine made by the claimed method can be used to prevent bacterial infections in humans, in particular *Moraxella catarrhalis* infections (page 1). The specification also teaches that there is no vaccine for *Moraxella catarrhalis* related diseases (page 2).

The specification fails to teach how to use the vaccine produced by the claimed method for protection against *Moraxella catarrhalis* infections. The term "vaccine" encompasses the ability of the specific antigen to induce protective immunity to a bacterial infection or disease induction. The specification does not provide evidence that the vaccines made by the claimed method are capable of inducing protective immunity. Examples 4-5 and 8 of the instant specification merely teach that vaccine produced by the claimed method can elicit antibodies when administered to a subject. However, there is no disclosure in the instant specification that vaccines produced by the claimed method can protect against *Moraxella catarrhalis* infections. This demonstration is required for the skilled artisan to be able to use the vaccines made by the claimed method for their intended purpose of preventing bacterial infections. Without this demonstration, the skilled artisan would not be able to reasonably predict the outcome of the administration of vaccines produced by the claimed method, i.e. would the vaccine provide protective immunity to a subject after administration of the vaccine. The ability to reasonably predict the capacity of a single bacterial immunogen

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or combinations of immunogens to induce protective immunity from *in vitro* antibody reactivity studies is problematic. Ellis (*Vaccines*, W.B. Saunders Company, 1988, Chapter 29) exemplifies this problem in the recitation that "the key to the problem (of vaccine development) is the identification of a protein component of a virus or microbial pathogen that itself can elicit the production of protective antibodies"(page 572, second full paragraph). Unfortunately, the art is replete with instances where even well characterized antigens that induce an *in vitro* neutralizing antibody response fail to elicit *in vivo* protective immunity. Boslego et al (*Vaccines and Immunotherapy*, Pergamon Press, 1991, Chapter 17) teach a single gonococcal pilin protein wherein the protein fails to elicit protective immunity even though a high level of serum antibody response is induced (page 212, bottom of column 2). Accordingly, the art indicates that it would require undue experimentation to formulate and use a successful vaccine without the prior demonstration of vaccine efficacy.

It is well known in the art that there are several different antigens from *Moraxella catarrhalis* (i.e. outer membrane proteins, lipooligosaccharides). It is also taught that since infections caused by *Moraxella* predominately occur on mucosal surfaces, the mucosal immune response is likely important as the first line of defense. Mucosal or surface antigen immune response would likely be important in the search for candidate vaccines (Kyd et al. 2000). It has also been recognized in the art that there is currently no vaccine to prevent *Moraxella catarrhalis* infections because of a lack of good animal models for the diseases, a lack of information about the protective antigens, a lack of *in vitro* correlates to immunity against *Moraxella catarrhalis* in humans and the

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pathogenic mechanisms and host immune response to the pathogens has yet to be clarified (Chen et al. 1996; Gu et al, 1998, Hu et al. 2000; Samukawa et al 2000 and Kyd et al 2000). While studies have been shown that the outer membrane proteins can elicit bacterial antibodies, which promote bacterial clearance, the results have not lead to a predictable vaccine against infections caused by *Moraxella catarrhalis*. A similar situation exists with the development of lipooligosaccharides (LOS) based vaccines against infections caused by *Moraxella catarrhalis*. Clearly a great amount of experimentation would be necessary in order to develop an efficacious vaccine against *Moraxella catarrhalis* infections.

Factors to be considered in determining whether undue experimentation is required, are set forth in In re Wands 8 USPQ2d 1400. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

Applying the above test to the facts of record, it is determined that 1) no declaration under 37 C.F.R. 1.132 or other relevant evidence has been made of record establishing the amount of experimentation necessary, 2) insufficient direction or guidance is presented in the specification with respect to producing a vaccine that would achieve a desire level of success when administered to a patient with a bacterial infection that is capable of preventing bacterial infection, 3) there are no working examples that the vaccine produced by the claimed method can be used to prevent

*Moraxella catarrhalis* infections, 4) the nature of the invention involved the complex and incompletely understood area of protective immune responses against *Moraxella catarrhalis* 5) the state of the prior art shows the lack of correlates to immunity with *Moraxella catarrhalis*, 6) the relative skill of those in the art is commonly recognized as quite high (post - doctoral level), and the lack of predictability in the field to which the invention pertains is recognized in the art as evidenced by the cited prior art.

In view of all of the above, in view of the lack of predictability in the art, it is determined that it would require undue experimentation to use the vaccine produced by the claimed method to protect a subject against infections caused by *Moraxella catarrhalis*.

5. No claims are allowed.

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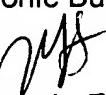
### ***Conclusion***

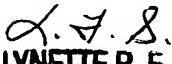
6. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 872-9306.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (571) 272-0857. The examiner can normally be reached on Monday – Friday from 9:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (571) 272-0864.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov/>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
Vanessa L. Ford  
Biotechnology Patent Examiner  
August 3, 2005

  
LYNETTE R. F. SMITH  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600